

## **REMARKS**

Claims 1-10 and 55-59 are currently pending in the application. Claims 1 and 4 are amended herein. Claim 1 is amended to remove claim language relating to variants of a HECT E3 ubiquitin ligase domain or Smad PY motif. Claim 4 is amended to add SEQ ID NO: 17, and to correct the sequence of SEQ ID NO:16 as recited. Support for this amendment is found in the specification at least at page 14, lines 26-30. No new matter has been added by way of this amendment.

Pursuant to 37 C.F.R. § 1.116(b)(1) and (2), Applicants submit that the present amendment is made to comply with the requirements of form expressly set forth in the previous Office Action and place the claims in better form for allowance or appeal. Therefore entry of this amendment after final action is respectfully requested. Upon entry of this amendment and remarks, claims 1-10 and 55-59 will be pending.

Applicants respectfully request reconsideration of claims 1-10 and 55-59.

### **Rejection Under 35 U.S.C. § 112, First Paragraph (Enablement)**

The Examiner has rejected claims 1-10 and 55-59 under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification. The Examiner, while stating that the specification is enabling for methods using a HECT E3 ubiquitin ligase domain, contends that the specification does not reasonably provide enablement for methods using variants of either such a domain or of a polypeptide comprising such a domain. Office Action at page 3. Applicants traverse as follows.

With regard to the enablement requirement of 35 U.S.C. § 112, first paragraph, M.P.E.P. § 2164.01 states, “[a]ny analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims so as to enable one skilled in the pertinent art to make and use the claimed invention.”

Without conceding the propriety of the Examiner’s rejection, Applicants have amended claim 1 to no longer recite “variants” of either a HECT E3 ubiquitin ligase WW domain or a Smad PY motif. Claim 1 as amended is enabled. The specification as originally filed explicitly teaches specific polypeptide sequences comprising a HECT E3 ubiquitin ligase WW domain. *See e.g.*, page 10, lines 13-20 (SEQ ID NO:1); and page 13, line 15 to page 14, line 10 (SEQ ID NOS: 3-13). The specification also explicitly teaches specific polypeptide sequences comprising a Smad PY motif. *See e.g.*, page 14, line 18 to page 15, line 4 (SEQ ID NOS: 14-25). Thus, the specification clearly describes the structural characteristics of polypeptides comprising an HECT E3 domain or a Smad PY motif so that

one of skill in the art would be able to practice the invention of claims 1-10 and 55-59. The Examiner does not point to any specific language in claims 2-9 or 55-59 in the rejection; thus, Applicants assume that the amendment to claim 1 is sufficient and that claims 2-10 and 55-59 are fully enabled by the specification, as well.

For the above reasons, Applicants respectfully request that the Examiner withdraw this rejection of the claims.

**Rejection Under 35 U.S.C. § 112, First Paragraph (Written Description)**

The Examiner has rejected claims 1-10 and 55-59 under 35 U.S.C. § 112, first paragraph. The Examiner alleges that while the claims encompass a large genus of variants, the specification fails to provide sufficient identifying characteristics of the variants to show that applicants were in possession of the claimed genus. Office Action at page 8. Applicants traverse as follows.

The written description requirement under the first paragraph of 35 U.S.C. § 112 requires the applicant to convey with reasonable clarity to those of skill in the art that, as of the filing date sought, he was in possession of the invention, *i.e.*, whatever is now claimed. *Vas-Cath Inc. v. Mahurkar*, 19 U.S.P.Q.2d 1111, 1117 (Fed. Cir. 1991). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams and formulas that fully set fourth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997).

Without conceding the propriety of the Examiner's rejection, Applicants have amended claim 1, as noted above, to delete reference to "variants" of the HECT E3 ubiquitin ligase domain and Smad PY motif. The subject matter of amended claim 1 is adequately described in the specification. The specification describes a consensus HECT E3 WW domain sequence (SEQ ID NO:2) (*see* page 13, lines 15-25) and includes a list of eleven representative HECT E3 ubiquitin ligase WW domains (SEQ ID NOS: 3-13) that may be used in the claimed methods. *See* page 13, line 26 to page 14, line 10. Further, the specification describes a minimum Smad PY motif sequence (SEQ ID NO: 14), a consensus sequence (SEQ ID NO:15) (*see* page 14, lines 18-21) and includes a list of eight representative Smad PY motifs (SEQ ID NOS:16, 17, 20, 21, 22, 23, 24 and 25) that may be used in the claimed methods. *See* page 14, line 26 to page 15, line 4. Thus, the specification clearly describes each and every one of the sequences recited in the claims, and thus conveys to one having skill in the art that they were in possession of the claimed invention at the time the application was filed. The Examiner does not point to any specific language in claims 2-

9 or 55-59 in the rejection; thus, Applicants assume that the amendment to claim 1 is sufficient and that claims 2-10 and 55-59 are fully described by the specification, as well.

For the above reasons, Applicants respectfully request that the Examiner withdraw this rejection of the claims.

### **Rejection Under 35 U.S.C. § 103**

The Examiner has rejected Claims 1, 2, 4 and 55 under 35 U.S.C. § 103(a) as being unpatentable over Pirozzi *et al.* (U.S. Patent No. 6,011,137) (“Pirozzi”) based on the recitation of “variant thereof.” Office Action at page 11. Applicants traverse as follows.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. M.P.E.P §2143, at 2100-126.

The Examiner contends that Pirozzi teaches a “variant” of the recited polypeptides, *i.e.*, a sequence having only 75% sequence identity to the WW domain sequence set forth in SEQ ID NO: 2, or a variant of sequence set forth in SEQ ID NOS:15, 16 and 18 (Smad PY motif). Office Action at page 11. Pirozzi does not teach or suggest any of the specific polypeptides recited in claim 1. As noted above, without conceding the propriety of the Examiner’s rejection, Applicants have amended claim 1 to no longer recite “variants” of the specified polypeptides. As such, Pirozzi fails to teach any of the sequences recited in amended claim 1 and, therefore, fails to teach the method of claim 1. Because Pirozzi fails to teach all of the limitations of amended claim 1, claim 1 is not obvious over Pirozzi. *See In re Gartside*, 53 U.S.P.Q.2d 1769 (Fed. Cir. 2000). As each of the remaining rejected claims ultimately depends from claim 1, these claims are also not obvious over Pirozzi.

Further, nothing in Pirozzi, or in the art, provides any motivation to modify the teachings or suggestions of Pirozzi to obtain the claimed invention. For example, Pirozzi contains no teaching or suggestion that a polypeptide comprising a HECT E3 ubiquitin ligase WW domain, or a polypeptide comprising a Smad PY motif, should be used in the methods and assays of Pirozzi to screen for agents that specifically modulate BMP-mediated signaling. Thus, a person of skill in the art would not be motivated to use the teachings or suggestions of Pirozzi to obtain the claimed method.

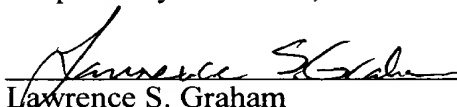
For the above reasons, Applicants respectfully request that this rejection of the claims be withdrawn.

### CONCLUSION

Applicants respectfully request that the above amendments and remarks and accompanying documents be entered in the present application file. An early allowance of the present application is respectfully requested. No fee, other than an extension-of-time fee, is believed due for this Amendment. However, if any fee is deemed to be due, please charge such fee to Jones Day Deposit Account No. 503013.

Respectfully submitted,

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